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EXAMINER	
SKOWRONEK, KARLHEINZ R	
ART UNIT	**PAPER NUMBER**
1631	

NOTIFICATION DATE	DELIVERY MODE
10/22/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPOPS.LEGAL@agilent.com

Office Action Summary	Application No.	Applicant(s)	
	10/821,829	MINOR, JAMES M.	
	Examiner	Art Unit	
	Karlheinz R. Skowronek	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 18-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

In view of the appeal brief filed on 25 June 2007, PROSECUTION IS HEREBY REOPENED. A new grounds of rejection is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

Claim Status

Claims 1-13 and 17-20 are pending.

Claims 14-16 and 21-34 are cancelled.

Claims 1-13 and 17-20 are being examined.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-13 and 17-18 are drawn to a process. A statutory process must include a step of a physical transformation, or produce a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). The instant claims do not result in a physical transformation, thus the Examiner must determine if the instant claims include a useful, concrete, and tangible result.

As noted in State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998) below, the statutory category of the claimed subject matter is not relevant to a determination of whether the claimed subject matter produces a useful, concrete, and tangible result:

> The question of whether a claim encompasses statutory subject matter should not focus on which of the four categories of subject matter a claim is directed to -- process, machine, manufacture, or composition of matter--but rather on the essential characteristics of the subject matter, in particular, its practical utility. Section 101 specifies that statutory subject matter must also satisfy the other "conditions and requirements" of Title 35, including novelty, nonobviousness, and adequacy of disclosure and notice. See *In re Warmerdam*, 33 F.3d 1354, 1359, 31 USPQ2d 1754, 1757-58 (Fed. Cir. 1994). For purpose of our analysis, as noted above, claim 1 is directed to a machine programmed with the Hub and Spoke software and admittedly produces a "useful, concrete, and tangible result." *Alappat*, 33 F.3d at 1544, 31 USPQ2d at 1557. This renders it statutory subject matter, even if the useful result is expressed in numbers, such as price, profit, percentage, cost, or loss.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific, and substantial. For a claim to be "concrete," the process must have a result that is reproducible. For a claim to be

"tangible," the process must produce a real world result. Furthermore, the claim must be limited only to statutory embodiments.

Claims 1-13 and 17-18 do not require the production of a tangible result in a form that is useful to the user of the process or apparatus. A tangible result requires that the claim must set forth a practical application to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment.

Claim 17 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claim is directed to a computer readable medium carrying instructions which when executed by one or more processors performs the steps of forming a plurality of characteristic signatures; providing a trend profile; performing statistical analysis; and rank ordering characteristic signatures.

The computer medium claimed has statutory and non-statutory embodiments. The specification discloses a non-limiting definition of computer readable medium that encompasses carrier waves as a medium for carrying the instruction [0077]. A carrier wave is not a tangible embodiment of the claimed readable medium and is further directed to a signal *per se* that is non-functional descriptive material, the claim is non-statutory.

> If the "acts" of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the acts are not being applied to appropriate subject matter. Gottschalk v. Benson, 409 U.S. 63, 71-72, 175 USPQ 673, 676 (1972). For purposes of an eligibility analysis, a physical transformation "is not an invariable requirement, but merely one example of how a mathematical algorithm [or law of nature] may bring about a useful application." AT &T, 172 F.3d at 1358-59, 50 USPQ2d at 1452. If USPTO personnel determine that the claim does not entail the transformation of an article, then USPTO personnel shall review the claim to determine it produces a useful, tangible, and concrete result. (MPEP 2106.02)

The process does not produce a physical transformation as the steps are directed to the transformation of data from one form to another. The process encoded in the medium produces a useful result to the extent that data relating to the determination of disease state is analyzed. The result of the executed process would produce a "concrete" or repeatable result, that is, given the same input data the executed steps would produce the same result each time the given set of data is used. The executed process does not produces a tangible result as a result of the transformation of the inputted data. Because the steps executed by the instructions encoded in the medium do not produce a result that is useful, concrete and tangible, the claim is rejected under 35 USC 101.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Singh et al. ("Gene Expression Correlates Of Clinical Prostate Cancer Behavior", Cancer Cell, Vol.1, March 2002).

The claims are drawn to a method for rank ordering characteristic signatures of cell properties, said method comprising the steps of: forming a plurality of characteristic signatures for a plurality of cell properties having been measured from a plurality of samples taken from a heterogeneous tissue region, wherein the heterogeneous tissue region includes a first portion having at least first and second types of tissue, bordered by a second portion, said second portion considered to be devoid of the second type of tissue, wherein the plurality of samples have been taken from successive locations along a determined profile of locations through the heterogeneous tissue region, with at least one sample being taken from the second portion, and wherein each of said characteristic signatures characterizing one of the plurality of properties, respectively; providing a trend profile of cell activity for the second type of tissue along the determined profile of locations through the heterogeneous tissue region; performing statistical analysis on each of the plurality of characteristic signatures with regard to the provided trend profile; and rank ordering the plurality of characteristic signatures based on proximity to the trend profile as determined by the statistical analysis.

Singh et al. teach a method for rank ordering characteristic signatures of cell properties. To summarize the teaching, Singh et al. have taken normal prostate tissue that is bordered on two sides by diseased tissue and performed gene expression

analysis and histological examinations of the samples resulting in a rank ordering of characteristic genes that can be used in the early diagnosis of prostate cancer.

The tissue used by Singh et al. is viewed as a heterogeneous tissue region (prostate, see figure 1 below) composed of two portions (Normal and Tumor, see figure 1 below). The first portion is composed of blood vessels and diseased tissue (Tumor) and the second portion is devoid of diseased tissue (Normal) ("Of these samples...", first paragraph, Tumor vs. normal classification, p.204). Based on a known trend for tumorous prostate to have a higher Gleason Score than normal or healthy prostate ("Gleason score", introduction, second paragraph, p. 203), Singh et al. performed histological examinations on a plurality of samples taken across the tissue to identify a characteristic signature Gleason score profile ("significant signature of GS", 3rd paragraph, Discussion, p.206). The gene models, provided in 4 and 16 gene models, of Signh et al. provided a trend profile of cell activity for the second type (diseased) of tissue along the profile of locations in the tissue (p 204, col. 1-2). The samples were also used to perform gene expression analysis. Resulting from the gene expression analysis was a rank ordering of signature genes ("Genes were ranked...", 2nd paragraph, Results: Tumor vs. Normal classification, p. 204). In the instant case, a plurality of cell properties is interpreted to include the individual expression states of a plurality of genes, i.e. a cell property can be the expression state of a particular gene, and thus a characteristic signature is a particular profile of expression for a gene or subset of genes in the context of a particular cell or tissue type. In the course of their gene expression analysis, Singh et al. formed a plurality of characteristic signatures

from a plurality of cell properties ("Type I" and "Type II", paragraph 2, Results: Prediction of Pathological features of Prostate Cancer, p. 204). Singh et al. performed statistical analysis on each of the plurality of characteristics signatures with regard to the provided trend profile. The statistical analysis was in the form of a correlation between the expression of particular genes and the Gleason score ("Correlations", Prediction of Pathological Features Of Prostate Cancer, p. 204). Singh et al. used two-step ranking procedure. In the first step, genes were ranked based on their expression relative to the tissue type (normal vs. diseased). In the second step, genes were ranked based on their correlation with the Gleason score to result in a "hierarchical clustering", interpreted as ranking ("A gene expression signature of GS...", second paragraph, Prediction of Pathological Features Of Prostate Cancer, p. 204). Singh et al. further illustrate the rank ordering of a plurality of characteristic signatures in figure 3 (p. 207).

Regarding claim 2, Singh et al. teach the step of measuring the plurality of cell properties for each of the plurality of samples. Singh et al. measured among others prostate serum antigen Gleason score, seminal vesicle invasion, gene expression, and pathological stage (Table 1, p. 205 and fig 1, p. 206).

Regarding claim 3, Singh et al. teach the steps of: providing the heterogeneous tissue region: and taking the plurality of samples from the heterogeneous tissue region, "...samples of prostate tumors and adjacent prostate tissues not containing tumor...were collected" (Prostate tissue samples, p. 208) (see also figure 1 of this office action).

Regarding claim 4, Singh et al. teach the step of: measuring the plurality of cell properties for each of the plurality of samples (Gene expression measurements, p. 208). "High-quality expression profiles were successfully derived ... using oligonucleotide microarrays containing probes for approximately 12,600 genes..."(Results, Tumor vs. Normal classification, first paragraph, p. 204).

Regarding claim 5, normalizing with respect to baseline established using healthy tissue, Singh et al. teach 317 genes had higher expression in tumor samples ("analysis", Results: Tumor vs. Normal classification, second paragraph, p. 204).

Regarding claim 6, Singh et al. teach the step of performing statistical analysis includes: comparing each of the plurality of characteristic signatures with the provided trend profile by curve-fitting to a statistical regression function, wherein said curve-fitting determines the degree of proximity of each of the plurality of characteristic signatures to the provided trend profile ("K-nearest neighbor (k-NN) class prediction models", p. 208).

Regarding claim 7, Singh et al. teach the step of performing statistical analysis includes: calculating a p-value with regard to each of the plurality of characteristic signatures, to test the null hypothesis between each of the plurality of characteristic signatures and the provided trend profile ("P-values", Experimental Procedures, in Correlation Of Gene Expression With Continuous Variables, p. 208; and in Gene Ranking, Class Prediction By *K*-Nearest Neighbors And Permutation Testing For Dichotomous Variables, p. 208).

Regarding claim 8, the statistical analysis is done in one two or three-dimensional space, Singh et al. teach the S2N statistical technique.

Regarding claim 9, Singh et al. teach the first type of tissue is healthy tissue ("not containing tumor", Experimental Procedure, Prostate Tissue Samples, p. 208).

Regarding claim 10, Singh et al. teach the second type of tissue is diseased tissue ("prostate tumors", Experimental Procedure, Prostate Tissue Samples, p. 208).

Regarding claim 11, Singh et al. teach one of the plurality of properties is an expression level of a gene (gene expression measurements, p. 208).

Regarding claim 12, Singh et al. teach the step of measuring a plurality of properties includes: processing each of the plurality of samples using a microarray technique ("U95Av2 arrays", gene expression measurements, p. 208).

Regarding claim 13, the step of measuring a plurality of properties includes: processing each of the plurality of samples on a single two-color microarray, two single-color microarrays or both is inherent to the teaching of Singh et al. It is understood in the art that the application of microarrays to measure gene expression requires the use of minimally 1 labeled sample and more commonly involves the use of 2 differentially labeled sets of probes thus the number of colors used in a microarray experiment is an intrinsic property of the microarray.

Response to Arguments

Applicant's arguments filed 25 June 2005 have been fully considered but they are not persuasive.

Regarding the rejection of claims 1-13 under 102(b) over Singh et al, Applicant argues that the prior art fails to teach the limitation of a plurality of characteristic

signatures from measurements taken from samples taken from successive locations along a determined profile of locations through the heterogeneous tissue.

Singh et al. teaches taking a plurality of samples from tissue obtained from radical prostatectomy (208, col. 1, prostate tissue samples, line 1-3). Prostatectomy is the removal of the heterogeneous tissue known as the prostate which is composed of a plurality of tissue types, for example blood vessels, muscle, epithelial, and nerve. The embedded sample of Singh is composed of two portions: a first portion composed of a first tissue, blood vessels, and a second tissue, tumor tissue, and a second portion devoid of the second type of tissue, tumor, i.e. normal (see figure 1 above). Singh et al. shows that of 253, 65 prostate specimens were determined to have tumor on opposing sides of the specimen and 52 were used to in the analysis (204, col. 1, results tumor vs normal classification, line 5-6, p208, col. 1, Prostate tissue samples, lines 4-5). This is interpreted to mean that normal tissue was bounded on opposite sides by tumorous tissue in the removed prostate specimen (figure 1 above) and reads on the limitation of a "heterogeneous tissue region". Further giving the claims their broadest reasonable interpretation, the teaching of Singh et al. taking two samples, one of normal tissue and one of diseased tissue, from each of the 52 prostates obtained teach the limitations of

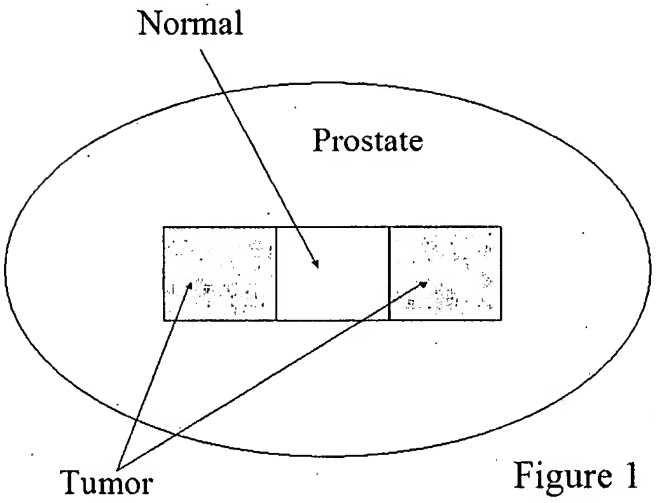

Figure 1

the claims reciting a "plurality of samples from". Singh et al. teach obtaining gene expression profiles from tumor and normal tissue samples using microarrays of 12,000 genes (p. 204, col. 1, results tumor vs normal classification, line 6-11). The 12,000 genes on the array are viewed to read on the plurality of properties recited in the claims. The gene expression recited by Singh et al. reads on the characteristic signature as instantly claimed. Singh et al. make correlation between Gleason score (GS) and the measured gene expression profiles. Teaching specifically that a readily detectable and statistically significant signature of GS exists (p. 206, col. 1, para. 2, line 7-9). Singh et al. also teach gene expression signature profile composed of a plurality of gene expression signatures of GS (p. 204, col. 2 para. 2, lines 1-5). Singh et al. provide a trend profile for the second type of tissue and perform a statistical analysis on each of the characteristics signatures First, Singh at al. teach profile of a second tissue determined along the profile of locations in providing a "normal" gene expression profile (p. 204, col. 1, results tumor vs normal classification, lines 8-10). Second, the statistical comparison between the particular gene measures in normal versus tumor tissue (p. 204, col. 1, results tumor vs normal classification, para 2, line 3-7). Third, Singh et al. teach ranking the profile signatures (p. 204, col. 1, results tumor vs normal classification, para 2, line 1-3). Thus providing rank ordered characteristic signatures as in claim 1.

Applicant also argues that the expression profiles of Singh et al. are not anticipatory of the instantly claimed characteristic signatures. This is not found persuasive. The specification does not explicitly define "characteristic signatures". The

specification recites "characteristic signatures characterize one of the plurality of properties" and characteristic signatures are formed using the measured plurality of properties" (specification, [0006] line 7-8). A gene is interpreted to be a property and gene expression is interpreted to be a characteristic signature. Based on the guidance provided by the specification, Singh et al. teaches obtaining gene expression data (characteristic signatures) from normal and tumorous samples for 12,000 genes (properties). The samples in Singh et al. are taken from predetermined locations in the prostate specimen because the samples were taken from regions in the specimens that were tumorous and non-tumorous.

Applicant argues that Singh et al. does not show providing a trend profile. This is not found persuasive because Singh et al. shows the formation and provides models of 4 or more genes, specificically 4 and 16 gene models (i.e trend profiles) that are used to identify and differentiate normal from diseased (p. 204, col. 1-2).

Applicant argues that no trend profile is used to compare any characteristic signature. The specification teaches the trend profile is typically known from a conceptual knowledge of the disease state and that the comparison involves comparing the trend profile with each differential expression signature using statistical analysis (Specification, [0058], sentences 1-2). In view of the guidance from the specification, Singh et al. teach the correlation of the differential gene expressions signatures to the trend profile of the of the Gleason score (GS), an indicator of prostate cancer progression (p. 204, col 2, "prediction of pathological features...", para 2, lines 2-5).

Applicant argues that the instant invention is further distinguished from Singh et al. because the instant invention takes samples from successive locations of the same heterogeneous tissue region. Analogous to the instant invention, Singh et al. takes samples from two successive locations from the same prostate specimen.

Thus the rejection of claims 1-13 as anticipated by Singh et al. under 35 USC 102(b) is maintained.

The following rejection is maintained from the previous office action.

Claims 1-10, 12-13, and 17-20 rejected under 35 U.S.C. 102(e) as being anticipated by Crosby et al. (US PG Pub 2003/0190689).

The claims are drawn to a method for rank ordering characteristic signatures of cell properties, said method comprising the steps of: forming a plurality of characteristic signatures for a plurality of cell properties having been measured from a plurality of samples taken from a heterogeneous tissue region, wherein the heterogeneous tissue region includes a first portion having at least first and second types of tissue, bordered by a second portion, said second portion considered to be devoid of the second type of tissue, wherein the plurality of samples have been taken from successive locations along a determined profile of locations through the heterogeneous tissue region, with at least one sample being taken from the second portion, and wherein each of said characteristic signatures characterizing one of the plurality of properties, respectively; providing a trend profile of cell activity for the second type of tissue along the determined profile of locations through the heterogeneous tissue region; performing

statistical analysis on each of the plurality of characteristic signatures with regard to the provided trend profile; and rank ordering the plurality of characteristic signatures based on proximity to the trend profile as determined by the statistical analysis.

Cosby et al. teach method of identification of the most relevant biomarkers of disease progression. In their method, Crosby et al. form a plurality of characteristic signatures of plurality of cell properties measured from a plurality of samples taken from a heterogeneous tissue region. In Crosby et al. the plurality of samples is from a heterogeneous tissue region are in the form of multiple sequential tissue slices ("cellular assays...", [0080], p. 9). The sequential tissue slices are cross-sectional tissue samples analogous to the sampling points 108a-n exemplified in figure 1 of the instant application. Crosby et al. analyze the cells that compose the sequential tissue slices by immunohistochemistry (IHC) using antibodies recognizing the phosphorylation state of signal transduction proteins ("...phospho-specific antibodies...", [0025], p. 3 and [0081], p. 9). Crosby et al. disclose samples having negative and positive disease outcomes ("...samples from patients having negative...", [0025], p. 3) is viewed to read on heterogeneous tissue region including a first portion having at least a first and second types of tissue, bordered by a second portion considered to be devoid of the second type of tissue. Tissue that has a negative disease outcome is normal, whereas tissue that has a positive disease outcome is diseased. Crosby et al. provide a trend profile of cell activity for the second type of tissue by hypothesizing the disease involves altered signal transduction ("...down stream pathway markers...", [0008], p. 1 and "...altered signal transduction", [0025], p. 3). Crosby et al. perform statistical analysis on each of

the plurality of characteristic signatures with regard to the trend profile by establishing a "significant correlation" based on the statistically difference between a characteristic signature compared to an outcome than to random chance ("significant correlation", [0043], p. 5). In Crosby et al., the characteristic signatures are rank ordered based on proximity of to the trend profile as determined by the statistical analysis using statistical clustering techniques to identify the best (highest rank) characteristic signature associated with disease outcome ("Such correlation analysis...", [0094], p. 9).

Regarding claims 2 and 4, Crosby et al. measure the plurality of cell properties for each of the plurality of samples through the use of a plurality phospho-specific antibodies to detect the phosphorylation statuses of a plurality of signal transduction proteins ("Such panels...", [0060], p. 6).

Regarding claim 3, providing the heterogeneous tissue region and taking a plurality of samples, Crosby et al. teach obtaining cellular samples from a plurality of patients ("...obtaining...", [0025], p. 3).

Regarding claim 5, normalizing the characteristic signature to a baseline, Crosby et al. teach altered activity (relative to the non-diseased state) ([0033], p. 4 and claim 26, step c).

Regarding claim 6 and 7, comparing each of the plurality of characteristic signatures with the trend profile and calculating a p-value, Crosby et al. teach the chi-squared statistical test ("Chi-squared tests" and "P-value", [0043], p. 5).

Regarding claim 8, the statistical analysis is done in one two or three-dimensional space, Crosby et al. teach the Chi squared test as noted above and a multi dimensional plot in figure 3a that is based on the cluster analysis statistical technique.

Regarding claim 9 and 10, the first type of tissue is healthy tissue and the second type of tissue is diseased tissue, Crosby et al. teach the samples from patients having negative and positive disease outcomes, which is viewed as the first type of tissue is healthy tissue and the second type of tissue is diseased tissue. Tissue that has a negative disease outcome is healthy (non-diseased), whereas tissue that has a positive disease outcome is diseased ("...samples from patients having negative...", [0025], p. 3).

Regarding claim 12, processing the plurality of samples using a microarray technique, Crosby et al. teach the application of a tissue microarray ("tissue microarray", [0078], p. 8).

Regarding claim 13, a single two-color microarray or two single-color microarrays or both. Since in a tissue micro array the tissue samples are bound to a solid support, a plurality of probes (antibodies in the case of Crosby et al.) labeled with a plurality of chromophores can be used to detect the presence of the target.

Regarding claim 17 and 18-20, a computer readable medium carrying instructions or a system for performing rank ordering by the steps of forming a plurality of signatures, providing a trend profile performing statistical analysis and rank ordering, Crosby et al. teach the automated analysis of stained tissues or cells ("Scoring" and "automatic cell staining instruments", [0077], p. 8 and "...using statistical software...",

[0091], p. 9). The implementation of microprocessors is an inherent property of any automated system in biotechnology; accordingly, necessary to the particular automated system is a computer readable medium to provide the instructions to the microprocessor. The computer readable medium could be, for example, magnetic disk, optical disk, or IC chip.

Response to Arguments

Applicant's arguments filed 25 June 2007 have been fully considered but they are not persuasive.

Regarding the rejection of claims 1-10, 12-13 and 17-20 as anticipated by Crosby et al. under 35USC102(e).

Applicant argues that Crosby et al. does not teach the limitations of the independent claims 1, 17, and 18. This is not found persuasive.

Crosby et al. teach obtaining a plurality of samples from patients having positive and negative disease outcomes [0025] reading on the plurality of samples. Crosby then detects the phosphorylation statuses of a plurality of signaling proteins [0025] reading on forming a plurality of characteristics. Reading on the limitation of measuring from a plurality of samples take from a heterogeneous tissue region, Crosby et al. teach the analysis of multiple sequential tissue slices [0080]. Crosby et al. teach determining the correlation of protein activity (characteristic signature) and a disease outcome (trend profile)[0092] and identification of the best (most highly correlated, i.e. rank ordered) biomarkers [0094] reading on providing a trend profile, performing a statistical analysis

on each of the characteristic signatures with regard to the trend profile, and rank ordering the characteristic signatures.

With regard to the limitations of claim 17 of a computer readable medium and 18 a system, Crosby et al. teach automatic analysis using high-throughput automation [0013].

Thus the rejection of claims 1-10, 12-13 and 17-20 as anticipated by Crosby et al. under 35USC102(e) is maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karlheinz R. Skowronek whose telephone number is (571) 272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

9 October 2007

/KRS/
Karlheinz R. Skowronek
Assistant Examiner, Art Unit 1631

10 October 2007

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER

SPE, AU 1631